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## **Vision-related Quality of Life and Locus of Control in Type 1 Diabetes. A Multicentre Observational Study.**

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**Abstract.****Aims.**

Diabetic retinopathy remains asymptomatic until its late stages but remains a leading cause of vision impairment and blindness. We studied quality of life and the ability to deal with the discomfort deriving from the presence of a chronic disease in patients with Type 1 Diabetes and different stages of retinopathy.

**Methods.**

Multicenter collaborative observational study involving 9 centers screening for retinopathy in different areas of Italy. The National Eye Institute 25-item Visual Functioning Questionnaire and the Locus of Control tool were administered to 449 people with Type 1 diabetes between February 2016 and March 2018. Socio-demographic and clinical data were collected.

**Results.**

On multivariable analysis, severe retinopathy associated with worse scores for General Vision, Ocular Pain, Near Vision Activities, Distance Vision Activities, Driving, Color Vision, Peripheral Vision, and lower values of Internal Control, independently of visual acuity. Women had a perception of worse General Health, Distance Vision Activities and Driving, and lower Internal Control and Trust in Others. Worse scores for Visual Specific Social Functioning, Visual Specific Mental Health, Visual Specific Role Difficulties, Visual Specific Dependency and Peripheral Vision were associated with higher HbA1c levels. Fatalism increased with rising HbA1c levels.

**Conclusions.**

These results confirm that a gap exists between patients' knowledge and expectations on retinopathy and providers' expertise and assumptions. To bridge this gap, patient-centered education and engaging approaches may be more effective than simple information given during consultations.

**Keywords**

Quality of life, people with type 1 diabetes, diabetic retinopathy.

## **Introduction.**

Diabetic retinopathy (DR) remains asymptomatic until it reaches its late stages but is still a leading cause of vision impairment and blindness in people with diabetes (1-3). The prevalence of DR is about 70 % in patients with type 1 diabetes and 40 % among those with type 2, with no differences by gender (3). Its annual incidence ranges from 2.2% to 12.7% and progression rate from 3.4% to 12.3% (3). Although optimal control of blood glucose and blood pressure can prevent DR and retard its progression, they are not always achieved (4). In addition, even among patients well within treatment targets, retinopathy may develop and progress (4). Hence, despite regular control visits, treatment by laser photocoagulation or other invasive therapies may become necessary (4-6).

Well-organized procedures to screen for sight-threatening DR reduce the risk of visual loss, and success of prevention strategies depends on planning and instrumentation as well as patient involvement (5,6). However, people with diabetes are not always able to understand the link between eye problems, poor metabolic control and the importance of regular eye exams (7). In addition, they may have difficulties in coping with the complications of DR (7), in terms of worsening visuo-specific quality of life, deterioration in social and relational aspects and daily tasks. All this may lead to depression, social isolation, and difficulties at home, in school, or at work. As a preliminary step to make integrated, people-centered health services work by fostering patient engagement (8), we studied quality of life and the ability to deal with the problematic situations that derive from the presence of a chronic disease in patients with Type 1 Diabetes and different stages of diabetic retinopathy.

## **Patients and Methods.**

This was a multicenter collaborative and observational study involving 9 centers dedicated to the screening of DR in different geographical areas of Italy. Patients attending their DR screening clinics were enrolled consecutively. Approval of the institutional Ethics Committees by Città della Salute e della Scienza di Torino, Ordine Mauriziano di Torino, was extended to all participating center. All patients signed their informed consent to participate.

Socio-demographic data were collected from digital medical records and are shown in Table 1. These include gender, age, Best Corrected Visual Acuity (BCVA), duration of diabetes, schooling, living alone, occupation, smoking habits, physical activity, presence of hypertension, HbA1c, frequency of self-monitoring of blood glucose, daily units of insulin, use of continuous insulin infusion and number of hypoglycaemic episodes or severe hypoglycaemias requiring administration of i.m. glucagon over the previous six months. Frequency of diabetes visits and eye visits over the previous year, reasons for eye consultation, severity of DR, cataract and previous laser treatment are also detailed in Table 1.

The patients were offered 3 options to answer the question about their reasons for attending the eye clinic: *Requested by diabetologist; Requested by the patient in the absence of visual symptoms; Requested by patient because of visual symptoms.*

Screening for DR was carried out according to Italian guidelines (9). Briefly, the procedure includes collection of patients' data, measurement of BCVA, pupil dilation by 1% tropicamide eyedrops, and colour photographs of 2 x 45° fields (macula and nasal to disc). The retinal photographs were graded by expert ophthalmologists in each centre, according to routine clinical practice, and DR was classified as: absent, mild (microaneurysms only or isolated blot haemorrhages) corresponding to ETDRS grade 20 (10), moderate (ETDRS grade 35), severe non proliferative (ETDRS grades 47-53), and proliferative. Previous laser treatment was assessed from the patient's history.

### ***Psychometric evaluation***

Two questionnaires, the National Eye Institute 25-item Visual Functioning (NEI VFQ-25) (11-13) and the Locus of Control tool (14), were administered to 449 people with type 1 diabetes, aged 18 - 80 years, attending DR screening clinics between February 2016 and March 2018.

The providers involved in the study were trained to follow the correct procedures for the administration of the questionnaires and collect variables.

The original NEI VFQ-25 Questionnaire had been translated into Italian and validated (13). It includes 25 items grouped into 12 subscales: *General Health, General Vision, Ocular Pain, Difficulty with Near-vision Activities, Difficulty with Distance-vision Activities, Vision Specific Social Functioning, Vision Specific Mental Health, Vision Specific Role Difficulties, Visual Specific Dependency, Driving Difficulties, Difficulty with Color Vision, Difficulty with Peripheral Vision.*

Each subscale is converted to a score between 0 and 100, higher scores indicating better vision-specific quality of life. The questionnaire takes on average approximately 10 minutes to administer in the interviewer format (13).

The Locus of Control questionnaire of Peyrot and Rubin includes a set of 18 statements measuring expectancies of Internal, Chance, and “Powerful Others” control over diabetes-related health outcomes. The final questionnaire consists of 6 items for each of 3 domains measuring the degree to which subjects consider their diabetes to be under their own control, dependent on others, or dependent on chance or fate (14).

After completing the questionnaires, the patients were given the opportunity to answer a final open question: *“Thank you for answering these questions and giving your opinion. If you wish to add further comments please write them on this page.”*

### ***Statistical analysis***

Results are shown as relative frequencies (%) for categorical data and mean  $\pm$  SD or median and interquartile range (IQR) for continuous variables, as appropriate.

The chi-square test for categorical variables and analysis of variance (ANOVA) with Bonferroni correction, or Kruskal-Wallis test in case of nonparametric distribution, for continuous variables were carried out to assess whether significant differences could be detected among 4 DR stages (*no; mild-moderate; severe; previous laser treatment*) for socio-demographic and clinical data, and to compare the above stages of DR for the items from the NEI VFQ-25 and Locus of Control questionnaires. Chi-square test for categorical variables and t or Wilcoxon test for continuous variables were used to compare the *severe DR* and *laser treatment* groups.

Multivariable analysis models were then used to investigate the independent effects of different stages of DR on vision-related quality of life and Locus of Control. Linear regression models were fit using scores from the different subscales of the NEI VFQ-25 and Locus of Control questionnaires as dependent variables and the 3 stages of DR severity (no, mild-moderate and severe), gender, duration of diabetes, schooling, smoking habits, hypertension and HbA1c as independent variables.

For all tests, a p-value of less than 5% was considered significant.

All analyses were performed with Stata 14.

## Results

Four hundred and forty-nine people with type 1 diabetes were recruited and administered the two questionnaires. Assessable fundus photographs were available for 443 of them, 156 with no retinopathy, 115 with mild-moderate retinopathy, 151 with severe retinopathy and 21 who had received laser treatment.

### *Socio demographic and Clinical data*

Table 1 shows that patients without DR were younger and had shorter disease duration ( $p<0.001$ ). People with Severe DR had worse BCVA ( $p<0.001$ ), longer diabetes duration ( $p<0.001$ ), were more likely to be hypertensive, had lower schooling and were more likely to be housewives/retired and self-employed ( $p=0.014$ ). As the severity of retinopathy progressed, the number of eye visits per year increased ( $p<0.001$ ), in most cases as a consequence of visual symptoms ( $p<0.001$ ).

Compared with the patients with severe DR, those who had received Laser Treatment were younger ( $41.6\pm12.0$  vs  $47.9\pm9.5$ ; 0.0063) and had shorter diabetes duration ( $28.8\pm12.4$  vs  $35.1\pm10.2$ ; 0.0038), but did not differ significantly for any of the other variables considered.

### *Psychometric evaluation.*

Compared to the patients with Severe DR, those who had received laser treatment had worse scores for General Health ( $42.5\pm24.5$  vs  $58.3\pm28.2$ ; 0.0183) and Visual Specific Dependency ( $91.2\pm20.3$  vs  $97.1\pm10.4$ ; 0.04). However, because of their small number, patients who had received laser treatment were not included in Table 2, summarizing the data on vision-related quality of life, and the following multivariable analysis (Table 3).

Compared with patients with no and mild-moderate DR, those with severe DR had worse scores for General Vision, Ocular Pain, Near Vision Activities, Distance Vision Activities, Driving, Color Vision, and Peripheral Vision ( $p<0.001$ ). Visual Specific Mental Health was significantly lower in the Severe compared to the Mild-Moderate DR group only (0.046).

In terms of Locus of Control, the patients with Severe DR had lower scores for Internal Control than those without DR.

On multivariable analysis (Table 3), General Vision ( $p<0.001$ ), Ocular Pain ( $p<0.01$ ), Near Vision Activities ( $p<0.05$ ), Distance Vision Activities ( $p<0.01$ ), Driving ( $p<0.05$ ), Color Vision ( $p<0.05$ ), and Peripheral Vision ( $p<0.001$ ) remained significantly worse in the people with Severe DR.

Adding BCVA as an independent variable to all the models did not change the overall results, except for Driving, which improved with better BCVA ( $\beta$  1.12  $p=0.02$ ), whereas Severe DR was no longer significant.

Multivariable analysis also showed that General Health ( $p<0.01$ ), Distance Vision Activities ( $p<0.001$ ) and Driving ( $p<0.01$ ) were lower among women. Interestingly, General Health improved with longer duration of disease ( $p<0.01$ ), while Driving worsened in the presence of hypertension ( $p<0.05$ ).

Visual Specific Social Functioning ( $p<0.05$ ), Visual Specific Mental Health ( $p<0.05$ ), Visual Specific Role Difficulties ( $p<0.05$ ), Visual Specific Dependency ( $p<0.001$ ), Peripheral Vision ( $p<0.05$ ) were negatively modified by increasing glycated hemoglobin levels.

The Locus of Control questionnaire showed lower values of Internal Control in the presence of Severe DR ( $p<0.01$ ). Lower levels of Internal Control ( $p<0.01$ ) and Trust in Others ( $p<0.05$ ) were observed among women. Lower Fatalism ( $p<0.01$ ) and Trust in Others ( $p<0.05$ ) were found among people with higher education. People with higher levels of Trust in Others were more frequently hypertensive patients ( $p<0.001$ ) and Fatalism increased with increasing glycated hemoglobin ( $p<0.05$ ).

## **Discussion.**

The NEI VFQ-25 has demonstrated consistency and validity to assess the impact of retinopathy on the life of people with diabetes in previous clinical studies (15,16). DR is a common, potentially blinding, microvascular complication and studies exploring psychological adjustment in diabetic individuals showed that even those with mild DR express feelings of uncertainty and vulnerability at the prospect of losing vision (17). Key risk factors include hyperglycaemia, dyslipidaemia, hypertension and long duration of disease as the majority of patients will have some degree of retinopathy after 20 years of diabetes (18-20).

Diabetic Retinopathy is classified into mild, moderate and severe non-proliferative or proliferative according to the presence and severity of microaneurysms, intraretinal haemorrhages, hard exudates, cotton wool spots, venous caliber abnormalities, intraretinal microvascular abnormalities and

appearance of fibro-vascular proliferations (21). Visual acuity and visual functioning are usually not affected in its mild and moderate stages. However, as the disease progresses to severe retinopathy, visual impairment may occur, resulting in difficulties with day to day tasks, driving and mobility (22). Few patients in this study had severe visual impairment despite retinopathy in different stages, severe in about one third of cases and already treated by photocoagulation in 21. However, the NEI VFQ-25 questionnaire was able to detect subtle abnormalities in most dimensions, confirming previous data in the literature. We could confirm a link between psychological dimensions and daily activities previously reported by other studies that have shown the high emotional and social impact of DR (23,24). Indeed, people with severe DR may experience pain and difficulties in carrying out ordinary accomplishments such as cooking or daily family endeavors. Severe DR modifies the ability to engage in Distance Activities and social life in such cultural behaviors as viewing a film or participating in a sporting event. In this study people with type 1 diabetes and severe DR face difficulties in their daily existence in terms of autonomous driving of motor vehicles, color discrimination and moving in space because of difficulties with peripheral vision (24). Recurrent thinking about visual difficulties in addition to the perception of widespread discomfort was associated with high levels of glycated hemoglobin (25).

Severe DR was associated with reduced Internal Control of diabetes. The concept of Locus of Control denotes a context of outer- or inner-directed behavior in various situations faced by patients in daily life. Individuals who firmly believe in their ability to cope with anything that might happen to them are regarded as having an internal locus of control. In contrast, placing responsibilities outside oneself is considered an externalized locus of control. As such, the locus of control plays a major role in driving emotional reactions and behavior. A high level of education seems to provide more conceptual sturdiness to cope with the disease, as perceived autonomy support, autonomy-driven motivation and self-perceived competence play a significant role in explaining self-esteem among adults with sub optimally regulated Type 1 diabetes (26, 27).

In this study, women were particularly affected in the dimension of Trust in Others, suggesting changes in their life of relationships and lack of network support useful to cope with the discomfort of the disease. A lady wrote *“Diabetes struck when I was 12. I reacted badly. I felt different and sick. It took a lot of time and a lot of psychotherapy to fix the problem. It is not true that you can have a normal life. With diabetes you may have a good life but only with commitment, consistency and help”*. That women experience more profound discomfort in the presence of a complication had already been reported (28). In this sense, psychological support is important to help people with type 1 diabetes overcome the stigma of chronicity, as disease management may be hampered if a central self-concept of illness prevails. Improvement in treatment satisfaction and impact of disease support the efficacy of



structured sustained educational processes, while increased self-esteem may be associated with strengthened problem-solving strategies (27,28). Both require patient-centered approaches.

The increased sense of Trust in Others related to hypertension, and a stronger sense of fatalism related to high levels of glycated hemoglobin suggest that people do not benefit from a tendency to completely delegate their health care to others (29). These observations indicate that tackling glycaemic control is important not only to avoid complications but also to prevent patients from resorting to avoidant coping strategies. Furthermore, given the interplay between perceived control and passive coping, intervention efforts should include both cognitive and behavioral components to be effective (29).

This study shows that patients with type 1 diabetes had not received optimal eye care on a regular basis, as in many cases the visit was a consequence of their own perception of having visual symptoms, while in other cases it was the patients themselves who requested to have their eyes checked in the absence of symptoms. Guidelines in Italy (9) recommend proactive regular screening at least every other year or more frequently in the presence of diagnosed DR, but many people with diabetes do not receive regular ophthalmological care aimed at preventing visual impairment and blindness (30). Some patients have developed sufficient self-management skills to make them decide to be seen by an ophthalmologist. Among the responses collected from people with diabetes in this study, a sentence is indicative *“I am aware of the risks and complications, but being careful and trying to maintain good control and a good relationship with your doctor helps to prevent both”*. Overall, however, the good levels of BCVA in this study suggest that a mix of patient- and doctor-directed eye care had resulted in the prevention of severe visual loss. Overall, the study supports the notion that both type 1 diabetes *per se* and DR modify the perception of quality of life. One of our patients wrote *“Managing diabetes is complex and 90% depends on active participation of the person with diabetes, how much he/she knows about and accepts the disease. If you know it, you can live better with diabetes. To deny it, is harmful!”*. Interestingly, many patients reported to have had hypoglycemic episodes in the previous six months, some of them severe enough to require glucagon injections. Although not associated with the psychological dimensions explored in this study, this confirms that severe hypoglycemia persists and remains a challenge for patients with type 1 diabetes across their life span. Severe DR adds to diabetes in causing discomfort for daily activities. Previous studies exploring psychological adjustment in diabetic individuals with visual impairment showed that people with diabetes express feelings of uncertainty and vulnerability (30). In our case series, women show a perception of worse General Health and pervasive existential distress in their ability to face social relationships.

This study has strengths and limitations. Among the former, a fairly large number of patients examined in a multicenter approach, likely to represent most regional situations in Italy. Limitations include the cross-sectional approach, which limits the possibility to detect cause-effect relationships. However

these results suggest that a wide gap exists between patients' knowledge and expectations on retinopathy on the one side, and health operators' expertise and assumptions on the other. This is a wider problem of organization in the delivery of health care to patients with chronic diseases, which poses problems even in the best organized programs to screening for DR (6). Possibly, to bridge this gap, patient-centered education and engaging approaches would be much more effective than simple information given during consultations (31).

### **Authors' Contribution**

M.T. designed and coordinated the study, researched and analyzed data, and wrote the manuscript; L.C. and F.C. analyzed data, and reviewed/edited the manuscript; S.B., S.O., MC.D, R.L., E.A., R.P., S.C., researched data and reviewed/edited the manuscript; S.R., S.V., F.B., E.B., A.M, P.F., O.D., S.M., contributed to discussion and reviewed/edited the manuscript. M.P. designed the study and reviewed/edited the manuscript.

All authors approved the final article.

### **Guarantor Statement**

M.T. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

### **Duality of Interest**

No potential conflicts of interest relevant to this article were reported.

### **Ethical approval**

All procedures performed in studies involving human participants were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

### **Informed consent**

Informed consent to inclusion in the study was obtained from all individual participants included in the study.

### **Prior presentations**

Parts of this study were presented in abstract form at the European Association for the Study of Diabetes (EASD) 53<sup>rd</sup> Annual Meeting 2017 Lisbon, and the 118<sup>rd</sup> Annual Meeting 2017 of Internal Medicine Society (SIMI) Italy.

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**Table 1. Socio-Demographic and Clinical data.**

Results are shown relative frequencies (%) for categorical data\* and as mean  $\pm$  SD for continuous variables<sup>§</sup>

	<b>Total (n=449)<sup>°</sup></b>	<b>Absent DR (n=156)</b>	<b>Mild-Moderate DR (n=115)</b>	<b>Severe DR (n=151)</b>	<b>Laser Treatment (n=21)</b>	<b>p value</b>
<b>*Gender</b> ( <i>men-women</i> )	51.0 – 49.0	48.7 – 51.3	54.8 – 45.2	51.7 – 48.3	47.6 – 52.4	0.785
<sup>§</sup> <b>Age</b> ( <i>years</i> )	42.4 $\pm$ 12.8	35.1 $\pm$ 12.8	44.8 $\pm$ 12.3	47.9 $\pm$ 9.5	41.6 $\pm$ 12.0	<b>&lt;0.001</b>
<sup>§</sup> <b>Duration of diabetes</b> ( <i>years</i> )	27.2 $\pm$ 13.0	17.4 $\pm$ 10.7	30.0 $\pm$ 11.0	35.1 $\pm$ 10.2	28.8 $\pm$ 12.4	<b>&lt;0.001</b>
<b>BCVA</b> <i>median (IQR)</i>	10 (9;10)	10 (10;10)	10 (9;10)	9 (7;10)	10 (9;10)	<b>&lt;0.001</b>
<b>*Schooling</b>	23.9-49.9-26.2	20.6-45.2-34.2	20.0-53.0-27.0	30.7-50.7-18.7	19.1-61.9-19.0	<b>0.036</b>
<b>*Living alone</b> ( <i>Yes</i> )	52.3	57.9	43.9	51.7	66.7	0.074
<b>*Occupation</b>	19.2 - 13.4 - 18.3 - 29.9 - 19.2	19.3-12.7-17.3- 21.3- 29.3	17.4 -10.4 - 21.7 - 37.4-13.0	21.2-15.9-17.2- 33.1- 12.6	14.3-19.0-14.3- 23.8- 28.6	<b>0.014</b>
<b>*Smoking</b> <i>No/Yes/Former</i>	62.2 - 23.9 - 13.9	64.7 - 28.2 - 7.1	55.6 - 25.2 - 19.1	64.4 - 18.1 - 17.5	57.1 - 33.3 - 9.5	<b>0.017</b>
<b>*Physical activity</b>	54.9 - 34.8 - 10.3	52.6 - 39.7 - 7.7	55.7 - 31.3 - 13	56 - 34 - 10	71.4 - 19.1 - 9.5	0.406
<b>*Hypertension</b>	34.5	25.7	35.1	42.0	40.0	<b>0.026</b>
<sup>§</sup> <b>HbA1c</b> ( <i>% of total Hb</i> )	7.8 $\pm$ 1.3	7.7 $\pm$ 1.5	7.8 $\pm$ 1.2	7.8 $\pm$ 1.1	8.5 $\pm$ 2.2	0.0922
<sup>§</sup> <b>HbA1c</b> ( <i>mmol/mol</i> )	61.8 $\pm$ 14.6	61.0 $\pm$ 15.6	61.6 $\pm$ 13.2	61.7 $\pm$ 12.3	70.2 $\pm$ 24.1	0.0836
<b>*Self-monitoring of blood glucose</b> ( <i>&gt;4 home tests</i> )	56.2	61.0	53.0	55.0	47.6	0.488
<b>Insulin therapy</b> ( <i>daily units</i> )	42.3 $\pm$ 20.0	38.8 $\pm$ 18.0	43.3 $\pm$ 18.0	44.6 $\pm$ 23.6	42.9 $\pm$ 13.7	0.0725
<b>*Insulin Pump</b>	25.8	33.5	20.5	26.3	15.0	0.066
<b>*Hypoglycaemia in the last six months</b>	71.2	68.2	67.5	78.2	66.7	0.158
<b>*Severe hypoglycaemia requiring i.m. glucagon</b>	7.7	7.9	5.3	7.3	23.8	<b>0.035</b>
<b>*Diabetes visits <u>previous</u> year</b>	5.8 - 37.6 - 56.6	7.1- 36.8 - 56.1	7.0 - 33.0 - 60.0	4.0 - 38.0 - 58.0	4.8 - 57.1 - 38.1	0.419
<b>*Eye visits <u>previous</u> year (<i>&gt;once per year</i>)</b>	40.0	9.1	39.8	69.8	52.4	<b>&lt;0.001</b>
<b>*Reason for eye consultation</b>	62.7 -10.1- 27.2	82.6 - 9.7 - 7.7	65.8 - 7.9 - 26.3	43.0 -13.9 - 43.1	42.9- 0 - 57.1	<b>&lt;0.001</b>

<sup>°</sup>data on Diabetic retinopathy available only for 443 patients

**BCVA:** *Best Corrected Visual Acuity*

**Schooling:** *Primary and Middle school/ High school/ University degree.*

**Occupation:** *Housewife and Retired/ Blue-collar worker/ White-collar worker/ Self-Employed/ Others.*

**Physical activity:** *Rarely/ 2/3 time at weeks/ Everyday*

**Diabetes visits per year:** *None / 1 - 2/ 3 or more.*

**Reason for eye consultation:** *Requested by diabetologist/ Requested by patient without visual symptoms/Requested by patient because of visual symptoms.*

**Table2. The National Eye Institute 25-item Visual Functioning and Locus of Control Questionnaires.** Results are shown as mean  $\pm$  SD and \*analysis of variance (ANOVA) test.

Questionnaires and Dimensions	Total (n=449) <sup>°</sup>	Absent DR (n=156)	Mild-Moderate DR (n=115)	Severe DR (n=151)	p-value*
<b>National Eye Institute 25-item Visual Functioning</b>					
General health	57 $\pm$ 25.1	54.4 $\pm$ 20.6	61.5 $\pm$ 25.5	58.3 $\pm$ 28.2	NS
General vision	63.9 $\pm$ 19.5	70.3 $\pm$ 18.5	64.9 $\pm$ 18.6	57.2 $\pm$ 17.9	<b>&lt;0.001<sup>^^</sup></b>
Ocular pain	88.9 $\pm$ 13.6	91.7 $\pm$ 11.1	90 $\pm$ 12.5	85.7 $\pm$ 15.1	<b>&lt;0.001<sup>^^</sup></b>
Near vision activities	91.2 $\pm$ 15.1	93.2 $\pm$ 12.7	94.2 $\pm$ 10.2	87.8 $\pm$ 18.0	<b>&lt;0.001<sup>^^</sup></b>
Distance vision activities	93.9 $\pm$ 11.5	95.1 $\pm$ 9.0	95.5 $\pm$ 10.0	91.8 $\pm$ 13.5	<b>0.008<sup>^^</sup></b>
Visual specific social functioning	98.2 $\pm$ 7.8	98.5 $\pm$ 6.9	99.2 $\pm$ 3.8	97.6 $\pm$ 9.0	NS
Visual specific mental health	86.4 $\pm$ 15.6	86.9 $\pm$ 14.4	89.2 $\pm$ 11.7	84.7 $\pm$ 16.5	<b>0.046<sup>^</sup></b>
Visual specific role difficulties	95.0 $\pm$ 13.9	96.4 $\pm$ 11.8	96.5 $\pm$ 9.4	93.0 $\pm$ 17.5	NS
Visual specific dependency	97.4 $\pm$ 10.8	97.8 $\pm$ 11.7	98.4 $\pm$ 6.9	97.1 $\pm$ 10.4	NS
Driving	92.3 $\pm$ 12.9	94.4 $\pm$ 9.0	94.1 $\pm$ 9.6	89.2 $\pm$ 14.9	<b>&lt;0.001<sup>^^</sup></b>
Color vision	98.1 $\pm$ 8.1	99.2 $\pm$ 4.4	99.6 $\pm$ 3.3	95.8 $\pm$ 12.4	<b>&lt;0.001<sup>^^</sup></b>
Peripheral vision	93.7 $\pm$ 15.7	96.9 $\pm$ 10.0	98.0 $\pm$ 8.2	87.2 $\pm$ 21.8	<b>&lt;0.001<sup>^^</sup></b>
<b>Locus of Control</b>					
Internal Control	27.5 $\pm$ 5.3	28.4 $\pm$ 5.2	27.5 $\pm$ 5.0	26.8 $\pm$ 5.6	<b>0.038<sup>§</sup></b>
Role of Chance	12.4 $\pm$ 5.2	12.4 $\pm$ 5.3	12.7 $\pm$ 4.8	12.3 $\pm$ 5.4	NS
Trust in Others	22.8 $\pm$ 5.5	22.6 $\pm$ 5.2	22.9 $\pm$ 6.1	22.9 $\pm$ 5.3	NS

<sup>°</sup> data used for DR sum up to 422, having left out 21 patients with laser treatment and 6 missing

<sup>^^</sup>significant differences detected between both *Severe vs No* and *Severe vs Mild-Moderate* retinopathy group

<sup>^</sup>significant differences detected between *Severe vs Mild-Moderate* retinopathy group

<sup>§</sup> significant differences detected between *Severe vs No* retinopathy group





**Table 3. Multivariable analysis – NEI VFQ-25 and Locus of Control questionnaires. Results of linear regression analyses for the different dependent variables.**

Dependent variable	Independent variables – $\beta$ (CI95%)								
	Diabetic Retinopathy (Ref. No DR)		Gender (Ref Males)	Diabetes Duration	Schooling (Ref. Primary-middle school)	Smoking (Ref. No)		Hypertension (Ref. No)	HbA1c
	Mild-moderate	Severe	Women	Years	High-univ	Yes	Former	Yes	(%)
National Eye Institute 25-item Visual Functioning									
General Health	2.8(-4.0;9.6)	-2.8(-9.9;4.3)	<b>-6.5(-11.4;-1.5)**</b>	<b>0.34(0.1;0.6)**</b>	-5.1 (-10.9;0.6)	-3.3(-9.3;2.7)	-5.2(-12.6;2.2)	2.9(-2.3;8.2)	-1.2(-3.2;0.9)
General Vision	-5.3(-10.7;0.1)	<b>-12.1(-17.9;-6.3)***</b>	-2.3(-6.3;1.7)	0.04(-0.1;0.2)	3.8 (-0.9;8.6)	1.3(-3.6;6.2)	-0.07(-6.0;5.9)	-2.1(-6.5;2.3)	-1.1(-2.8;0.6)
Ocular Pain	-2.2(-5.8;1.3)	<b>-6.0(-9.7;-2.3)**</b>	-1.2(-3.8;1.4)	0.09(-0.03;0.2)	1.9 (-1.1;5.0)	1.6(-1.5;4.7)	-0.96(-4.8;2.9)	-2.5(-5.2;0.2)	0.3 (-0.7;1.4)
Near Vision Activity	1.5(-2.3;5.4)	<b>-4.2(-8.3;-0.2)*</b>	-1.6(-4.4;1.2)	-0.000(-0.13;0.13)	-0.8 (-4.0;2.5)	0.3(-3.1;3.7)	-3.6(-7.7;0.6)	-1.2(-4.2;1.7)	-0.6 (-1.8;0.5)
Distance Vision Activities	-0.6(-3.4;2.2)	<b>-4.0(-7.0;-1.1)**</b>	<b>-3.7(-5.8;-1.7)***</b>	0.07(-0.02;0.2)	-0.4 (-2.8;2.0)	<b>2.5(0.02;5.0)*</b>	-1.2(-4.3;1.8)	0.5(-1.7;2.6)	-0.3(-1.2;0.5)
Visual Specific Social Functioning	0.6(-1.0;2.2)	-0.3(-1.9;1.3)	-0.9(-2.0;0.2)	-0.005(-0.06;0.05)	0.05 (-1.3;1.4)	0.6(-0.8;2.0)	-0.2(-1.9;1.5)	0.4(-0.8;1.6)	<b>-0.6(-1.1;-0.1)*</b>
Visual Specific Mental Health	2.3(-1.5;6.1)	-2.1(-6.1;1.9)	-2.3(-5.1;0.5)	0.01(-0.1;0.1)	-2.7 (-6.0;0.5)	3.2(-0.2;6.5)	-3.8(-8.0;0.3)	0.5(-2.5;3.4)	<b>-1.4(-2.5;-0.2)*</b>
Visual Specific Role Difficulties	0.5(-2.8;3.8)	-2.1(-5.5;1.3)	-2.3(-4.7;0.1)	-0.004(-0.1;0.1)	-1.6 (-4.3;1.2)	1.7(-1.1;4.6)	<b>-4.0(-7.5;-0.4)*</b>	-0.2(-2.7;2.3)	<b>-1.0(-2.0;-0.02)*</b>
Visual Specific Dependency	0.2(-2.2;2.6)	-0.6(-3.1;2.0)	-0.3(-2.1;1.4)	0.03(-0.05;0.1)	-1.7 (-3.7;0.4)	1.3(-0.9;3.4)	-1.4(-4.0;1.2)	-1.0(-2.8;0.9)	<b>-1.5(-2.2;-0.8)***</b>
Driving	0.2(-3.4;3.7)	<b>-4.3(-7.9;-0.7)*</b>	<b>-3.3(-5.9;-0.8)**</b>	-0.04(-0.1;0.1)	-1.5 (-4.4;1.5)	-0.8(-3.9;2.2)	0.3(-3.4;4.0)	<b>-3.4(-6.0;-0.8)*</b>	-0.2(-1.4;0.9)
Color Vision	0.7(-1.4;2.8)	<b>-2.5(-4.6;-0.3)*</b>	-0.2(-1.7;1.2)	-0.03(-0.1;0.05)	-0.8 (-2.6;0.9)	-0.6(-2.4;1.2)	-0.7(-2.9;1.5)	1.3(-0.3;2.9)	-0.5(-1.1;0.1)
Peripheral Vision	0.8(-3.2;4.8)	<b>-8.7(-12.9;-4.5)***</b>	-1.5(-4.4;1.4)	-0.05(-0.2;0.09)	3.1 (-0.3;6.4)	1.7(-1.8;5.2)	2.3(-2.0;6.7)	0.1(-2.9;3.2)	<b>-1.2(-2.4;-0.04)*</b>
Locus of Control									
Internal Control	-0.9 (-2.4;0.6)	<b>-2.0(-3.6;-0.5)**</b>	<b>-1.6(-2.6;-0.5)**</b>	0.02(-0.03;0.07)	-1.0(-2.2;0.2)	-0.3(-1.6;1.0)	0.1(-1.4;1.7)	0.08(-1.0;1.2)	-0.0(-0.4;0.4)
Role of Chance	0.07 (-1.4;1.6)	-0.4(-1.9;1.2)	0.9(-0.1;2.0)	-0.0(-0.05;0.05)	<b>-1.8(-3.0;-0.5)**</b>	0.6(-0.7;1.8)	0.4(-1.2;2.0)	-0.2(-1.3;0.9)	<b>0.5(0.03;0.9)*</b>
Trust in Others	0.2 (-1.2;1.7)	-0.03(-1.6;1.5)	<b>-1.3(-2.3;-0.2)*</b>	-0.0(-0.06;0.04)	<b>-1.4(-2.6;-0.1)*</b>	-0.6(-1.9;0.7)	-1.3(-2.9;0.3)	<b>1.8(0.7;2.9)**</b>	-0.2(-0.7;0.2)

Significance levels are represented as follows: \*p<0.05; \*\*p<0.01; \*\*\*p<0.001